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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CANELLA, KAREN A	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 05/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/814,661	ROTHSTEIN ET AL.	
	Examiner	Art Unit	
	Karen A Canella	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-15,17-19 and 21-36* is/are pending in the application.

4a) Of the above claim(s) *1-13 and 24-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *14,15,17-19 and 21-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 14, 15, 17 and 21 have been amended. Claims 16 and 20 have been canceled. Claims 1-15, 17-19 and 21-36 are pending. Claims 1-13 and 24-36, drawn to non-elected inventions, remain withdrawn from consideration. Claims 14, 15, 17-19 and 21-23 are under consideration.

2. The text of sections of Title 35, US Code not found in this action can be found in a previous Office action.

3. Claims 14, 15, 17-19, and 21-23 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. .

(A) As drawn to written description

The instant claims are method claims reliant upon the identity of homologues of SEQ ID NO:2. The specification fails to provide a written description of said homologs and further states that there are no known homologs of Sml1. The specification states that it is likely that a homolog of Sml1 will be identified in human as the subunits of ribonucleotide reductase in yeast are closely related to those of humans (page 26, lines 33-36). The specification further contemplates that homologues of Sml1, such as a human, microbial, plant or insect Sml1 are other embodiments of Sml1. The specification lacks adequate written description of the genus of homologues of Sml1.

The findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter

sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that

a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. The instant specification may provide an adequate written description of the homologues of Sml1 per Lilly by structurally

describing a representative number of homologues of Sml1 which features constitute a "substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not describe the homologues of Sml1 relied upon in the instant method claims or the pharmaceutical compositions of claims 21-23 in a manner that satisfies either the Lilly or Enzo standards. The specification does not provide the complete structure of homologue of Sml1 other than SEQ ID NO:2, nor does the specification provide any partial structure of such homologues, nor any physical, chemical or functional characteristics of the homologues coupled with a known or disclosed correlation between structure and function. Although the specification discloses a single member of this genus as SEQ ID NO:2, this does not provide a description of genus of homologs on which the instant method claims rely that would satisfy the standard set out in Enzo.

The specification also fails to describe the genus of homologs by the test set out in Lilly. The specification describes only a single member of the genus, SEQ ID NO:2. Therefore, it necessarily fails to describe a "representative number" of such members of the genus In addition, the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus."

Because the product to which the instant method clams rely is not adequately described, the methods are also not adequately described.

Further, clams 21-23 embody pharmaceutical compositions identified by the screening assay of claim 14. The genus is highly variant encompassing compounds which differ widely in structure from the fragments of Sml1 and include organic compounds, inorganic compounds, lipids, peptidomimetics and synthetic compounds as evidenced by claim 15. The genus thus comprise compounds having numerous functions part from the fragments of Sml1. The specification describes fragment so Sml1 as a member of this genus. However, this disclosure does not satisfy the written describe requirement of the pharmaceutical compositions of claims 21-23 by the standards set forth in either Lilly or Enzo. It is noted that because the compounds have yet to be identified, they cannot be characterized, and therefore the specification would not

be able to provide an adequate written description of compounds which are yet to be identified. amendment of claims 21-23 to limit the scope of the claims to consisting of fragments of SEQ ID NO:2 is recommended.

(B) As drawn to new matter

Claim 14 has been amended to qualify the compounds to which the cell is contacted as being determined to mimic the binding to the Sml1 protein to ribonucleotides reductase in the cell. The specification does not provide support for the addition of this step in the instant method claim, and applicant did not point to the page and line numbers of the specification where support could be found.

4. The rejection of claims 14, 15, 18 and 19 under 35 U.S.C. 102(e) as being anticipated by Li et al (U.S. 5,767,134) is maintained for reasons of record. Claims 21 and 22 are also rejected as being anticipated by Li et al.

Li et al disclose a method of decreasing the activity of ribonucleotide reductase in a human cell comprising the administration of 3-aminopyridine-2-carboxyaldehyde thiosemicarbazone or 3-amino-4-methylpyridine-2-carboxaldehyde thiosemicarbazone (column 1, lines 15-50 and column 2, lines 31-34 and column 4, lines 35-41). Li et al disclose pharmaceutical compositions comprising said compounds (column 9, line 27 to column 10, line 2) which include carriers for oral, topical , subcutaneous and intravenous administration, thus fulfilling the specific embodiments of claim 22. The compounds disclosed by Li et al inhibit the activity of ribonucleotide reductase. The reference does not specifically teach that the inhibition of the ribonucleotide reductase alters the interaction between said ribonucleotide reductase and Sml1, however, the administration of the compounds disclosed by Li et al result in inhibition of ribonucleotide reductase and a reduction in tumor growth which appears to have the same effect as the claimed alteration of the interaction between ribonucleotide reductase and Sml1 which reduces the rate of cell division. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of a compound which alters the interaction between ribonucleotide reductase and Sml1 resulting in a decrease in cell division rate. . In the absence of evidence to the contrary, the burden is on the applicant to prove that the

claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Applicant argues that Li et al cannot anticipate the instant claims because Li et al do not disclose SEQ ID NO:2. this has been considered but not found persuasive. The instant claims are drawn to contacting a cell with a compound that would mimic the binding of Sml1 to ribnucleotide reductase, wherein Sml1 is SEQ ID NO:2 or a homologue thereof. If the compounds disclosed by Li et al inherently mimic the binding of Sml1, or a homologue thereof, to ribonucleotide reductase, then the specific embodiments of the claims are fulfilled. It is not necessary to disclosure the sequence of SEQ ID NO:2. The compounds disclosed by Li et al inhibit the activity of ribonucleotide reductase. Therefore, it is likely that they compete with the binding of a homologue of SEQ ID NO:2 and thus "mimic" the binding of Sml1 on ribonucleotide reductase.

5. The rejection of claims 14, 15, 18 and 19 under 35 U.S.C. 102(e) as being anticipated by Cooperman et al (U.S. 6,030,942) is maintained for reasons of record. Claims 21 and 22 are also rejected as being anticipated by Cooperman et al (U.S. 6,030,942.

Cooperman et al disclose an assay for the identification of ribonuclease reductase peptidomimetic that are able to reduce the division rate of the cell (column 12, lines 55-58). Cooperman et al disclose pharmaceutical compositions for the aerosol, topical and intravenous administration of the peptidomimetics (column 40, lines 32-67), thus fulfilling the specific embodiments of claims 21 and 22. Cooperman et al disclose that it is desirable to inhibit the ribonuclease reductase of a pathological cell type of a human, such as a cancer cell (column 14, lines 17-19), thus fulfilling the specific embodiments of claims 18 and 19 drawn to mammalian cells and human cells, respectively. Cooperman et al do not specifically disclose that the peptidomimetic will alter the interaction between the ribonucleotide reductase and the Sml1 protein in the cell, however, this would be inherent in the method of Cooperman et al as the peptidomimetics would compete with ribonucleotide reductase for binding to Sml1.

Applicant argues that Li et al cannot anticipate the instant claims because Li et al do not disclose SEQ ID NO:2. this has been considered but not found persuasive. The instant claims

are drawn to contacting a cell with a compound that would mimic the binding of Sml1 to ribonucleotide reductase, wherein Sml1 is SEQ ID NO:2 or a homologue thereof. If the compounds disclosed by Cooperman et al inherently mimic the binding of Sml1, or a homologue thereof, to ribonucleotide reductase, then the specific embodiments of the claims are fulfilled. It is not necessary to disclosure the sequence of SEQ ID NO:2.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 14, 15, 18, 19 and 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Li et al (U.S. 5,767,134) in view of Brown et al (US 4,393,041).

Li et al teach a method of decreasing the activity of ribonucleotide reductase in a human cell comprising the administration of 3-aminopyridine-2-carboxyaldehyde thiosemicarbazone or 3-amino-4-methylpyridine-2-carboxaldehyde thiosemicarbazone (column 1, lines 15-50 and column 2, lines 31-34 and column 4, lines 35-41). Li et al disclose pharmaceutical compositions comprising said compounds (column 9, line 27 to column 10, line 2) which include carriers for oral, topical , subcutaneous and intravenous administration, thus fulfilling the specific embodiments of claim 22. The compounds disclosed by Li et al inhibit the activity of

ribonucleotide reductase. Li et al teach subcutaneous administration of said compounds. Li et al do not teach a subcutaneous implant which is a time-release implant.

Brown et al teach a method to administer an active biochemical agent to a living animal over a period of time by subcutaneously implanting in said animal a pellet comprising the active biochemical agents (claim 1).

It would have been prima facie obvious at the time the claimed invention was made to administer the compounds taught by Li et al by a subcutaneous implant. One of skill in the art would have been motivated to do so by the teachings of Li et al on the subcutaneous administration of the compounds and the teachings of Brown et al on the administration of a time release pellet comprising an active agent. One of skill in the art would be motivated to administer drugs over a period of time in order to increase the length of exposure to a given concentration of drug.

The Li et al reference does not specifically teach that the inhibition of the ribonucleotide reductase alters the interaction between said ribonucleotide reductase and Sml1, however, the administration of the compounds taught by Li et al result in inhibition of ribonucleotide reductase and a reduction in tumor growth which appears to have the same effect as the claimed alteration of the interaction between ribonucleotide reductase and Sml1 which reduces the rate of cell division. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of a compound which alters the interaction between ribonucleotide reductase and Sml1 resulting in a decrease in cell division rate. . In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

9. All other rejections and objections as set froth in the previous Office action are withdrawn.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10 a.m. to 9 p.m. M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571)272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.
05/16/2004

KAREN A. CANELLA PH.D
PRIMARY EXAMINER